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# The comparison of corneal endothelium morphology through specular microscopy in morbid obesity with healthy controls

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## ABSTRACT

**Aims:** To evaluate the morphological changes in corneal endothelial cells with morbid obesity, and to analyze the relationship between BMI and corneal endothelial features.

**Methods**: The central corneal thickness (CCT), the average endothelial cell density (ECD) (cell/mm²), average cell area (CA) (µm²), coefficient of variation of cell area (CV) - (CV: Standard deviation/CA) values were recorded via specular microscopy in morbidly obese patients and controls. The whole parameters were compared.

**Results:** The morbid obese patients had significantly thicker corneas (p=0.013), and significant loss of hexagonality (p=0.012) compared with controls, while there was no significant difference in ECD (p=0.311), CA (p=0.292), and CA (p=0.161). In linear regression analysis, there was no significant correlation between CCT, abdominal circumference, and the endothelium parameters.

**Conclusion:** Although BMI has the effect of changing corneal morphology, this change is not correlated with an increase in BMI.

**Keywords:** Morbid obesity, specular microscopy, corneal endothelium

## INTRODUCTION

Obesity has been recently a public health issue with an increased trend worldwide. Morbid obesity may affect the several layers of the eye, both isolated and due to systemic diseases.[1] According to the World Health Organisation (WHO), the definition of obesity is the accumulation of abnormal or excessive fat in adipose tissue.[2] A body mass index (BMI) (weight in kilograms (or pounds) divided by the square of height in meters – kg/m²) over 25 is considered overweight, and over 30 is obese.[3]

The adipose tissue has an active metabolism in obesity, and also releases systemic inflammatory cytokines actively.[1] The effect of obesity on ocular structures has been previously reported[4-6], and one of these tissue is cornea which includes the most of refractive power of total eye, and also provides optical clearance for vision. The maintenance of corneal clarity is related to the healthy function and normal morphology of hexagonal corneal endothelium cells.[7] The morphology of corneal endothelium can be displayed through specular microscopy while the function can be indirectly stated by central corneal thickness (CCT). Specular microscopy is a method that can quantitatively evaluate the endothelial cell layer, which is the most important layer in ensuring corneal transparency, in vivo. It has high reliability in repeated measurements.[9] With this method, an idea can be obtained about both the number of corneal cells and their morphology (polymegathism, polymorphism).[10]

According to our hypothesis, the morbid obesity which is known as increased inflammatory cytokine status may affect corneal endothelium and may cause damage in endothelium cell morphology that leads to increased CCT. In the light of these information, the aim of the study is to define morphological changes in corneal endothelial cells with obesity and to evaluate the relationship between BMI and corneal endothelial features. In our knowledge, this is the first report that reveals the relationship between corneal endothelium and obesity.

## METHODS

This cross-sectional study followed the tenets of the Declaration of Helsinki, and it was approved by the Balıkesir University Faculty of Medicine Clinical Researches Ethics Committee (Date: 09.10.2019, Decision No: 2019/136).

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Informed consent was obtained from all cases. The participants were selected from the morbidly obese patients who were admitted to the department of general surgery for bariatric surgery between December 2022 – October 2023. The morbid obesity was defined as the patients who have BMI >40 or ≥35 kg/m² when associated with comorbidities such as arterial hypertension, dyslipidemia, sleep apnea, or diabetes. The patients were directed to the department of ophthalmology after the demographical features, detailed anamnesis, routine hemogram, biochemical, and hormone tests were recorded and BMI and abdominal circumference (AC) were measured. The AC was measured is measured at the midpoint of the line between the rib or costal margin and the iliac crest in the midaxillary line. The age and sex-matched healthy participants who were admitted to the hospital for routine control with BMI within the normal limits were held as controls. The exclusion criteria were the blood test that was outside the normal limits (other than 3.4-9.6 103/µL for leukocytosis, 13.2-16.6 d/dL for hemoglobine, 74-100 mg/dL for blood sugar, >%5,7 HbA1C, >200 mg/dL for total cholesterol, >150 mg/dL for trigliserit, >5 mg/L C-reactive protein, abnormal liver and kidnet function tests according to the laboratory reference limits), refractive error of more than ±3D, the history of corneal or intraocular surgery, corneal opacity or dystrophy, any type of glaucoma, the presence of systemic rheumatological disease, diabetes mellitus, hypertension, cardiovascular or kidney disease, active or previous uveitis, contact lens usage, genetical or systemic inflammatory disease. After detailed ophthalmological examination including spherical equivalent (SE), best-corrected visual acuity (BCVA), and intraocular pressure (IOP) through Goldmann applanation tonometry; the corneal endothelial evaluation through specular microscopy was completed. The whole measurements have been achieved only from the right eyes of participants.

**Specular microscopy:**

The analysis of corneal endothelium has been completed through specular microscopy CEM-530 (Nidek Co, Ltd, Japan). The patients were asked to place his or her chin and head firmly on the device and look directly ahead during measurements. The device automatically focuses on the endothelial layer of the cornea and the image is automatically recorded when the clearest image was detected. All measurements were repeated three times by the same technician between 09:00 and 10:00. The average of the values was accepted as valid.

The CCT, the average endothelial cell density (ECD) (cell/mm²), average cell area (CA) (µm²), and coefficient of variation of cell area (CV)-(CV: Standard deviation/CA) values were recorded via specular microscopy. The CV is considered as an indicator of changes in CA and is defined as polymegathism. The percentage of cells with a hexagonal structure is defined by the hexagonality (HEX) parameter, and changes in these cell shapes are defined as polymorphism (Figure).

### Statistical Analysis

The statistical analysis were completed by using SPSS 23.0 program. The suitability of the data for normal distribution was evaluated with the Kolmogorov-Smirnov test. The results were expressed as mean ± standard deviation. Chi-square test was used for categorical variables such as gender. Independent samples t-test was used for comparisons on numerical variables between groups. Linear regression analyses were used to detect variability between parameters. A p value of less than 0.05 was considered statistically significant.

**Figure.** Specular microscopy screen output

## RESULTS

In the current study, 72 patients who had the diagnosis of morbid obesity were prospectively evaluated. Twelve of 72 patients had abnormal blood tests (7 of them had higher HbA1c, 5 of them had hypercholesterolemia) 8 of them had corneal opacity, and 2 of them had degenerative myopia. These patients were excluded according to the strict exclusion criteria. As a consequence, the study included 50 eyes of 50 patients with a mean age of 27.6±7.1 years in morbid obese group (Group 1) and 52 eyes of 52 patients with a mean age of 31.3±6.4 years in the control group (Group 2) (p=0.167). There was no significant difference between the groups in terms of gender (F/M: 18/32 and 15/37 in Groups 1 and 2, respectively; p=0.514). Among anthropometric measurements, BMI and AC were 45.9±2.7 and 137.2±4.5 kg/m² in Group 1, and 20.2±1.2 and 78.3±6.1 cm in Group 2 (p<0.001 for BMI and WC) respectively. In Group 1 and 2, the BCVA was 0.99±0.02 and 0.99±0.02 (p=0.806), IOP was 14.2±2.6 and 14.9±2.9 mmHg (p=0.557) and SE was 0.19±0.63 and 0.33±0.58 D (p=0.545) respectively the parameters in specular microscopy among groups were summarized in Table.

**Table. The comparison of corneal endothelial parameters between morbidly obese patients and controls**

| | Group 1 (n:50) | Group 2 (n:52) | p-value |
|---|---|---|---|
| **CCT** | 541.7 ± 34.6 | 514.5 ± 7.6 | 0.013* |
| **ECD (cell/mm²)** | 2273.6 ± 307.5 | 2385.8 ± 256.8 | 0.311 |
| **CA (µm²)** | 450.3 ± 76.3 | 423.7 ± 45.6 | 0.292 |
| **CV** | 37.1 ± 13.7 | 31.0 ± 5.1 | 0.161 |
| **HEX** | 42.9 ± 22.7 | 62.2 ± 21.0 | 0.012* |

CCT: Central corneal thickness, EHD: Endothelial cell density, CA: Cell area, CV: Coefficient of variation of cell area, HEX: Hexagonality
p-value: statistically significant ratio

In linear regression analysis, there was no significant correlation between CCT, AC, and CCT, EHD, CA, CV, and HEX. (BMI and CCT p=0.085, EHD p=0.274, CA p=0.334, CV p= 0.931, HEX p=0.061) (AC and CCT p=0.080, EHD p=0.148, CA p=0.281, CV p=0.980, HEX p=0.069).

## DISCUSSION

In this study, the central corneal thickness of morbidly obese patients was found to be significantly thicker compared to the controls. This difference was not related to the change in endothelial cell number. While a non-significant increase in endothelial cell area was detected in morbid obese patients, this did not lead to polymegatism. Although there was no compensatory increase in cell size, a significant loss of hexagonality was detected in the cell structures. Similarly, Bu et al.[8] detected a decrease in endothelial cell density and loss of hexagonality in rats that developed obesity as a result of feeding a hyperlipidemic diet. The authors attributed this situation to the loss of tight connections between corneal epithelial cells and increased oxidative stress in obesity. In our study, the increased CCT can be explained by the loss of epithelial tight junctions and the secondary relative corneal edema seen in the anterior layers of the cornea.

Corneal endothelial cells are most commonly affected by intraocular surgeries. It can lead to corneal decompensation with a significant decrease, especially after complicated cataract surgeries.[11] Even if there is no history of intraocular surgery, endothelial cell loss is observed at a rate of 0.6% annually with age.[12,13] In our study, a significant increase in corneal thickness, which is an indirect indicator of corneal endothelial cell function, was detected in obese patients. This situation is independent of the number of endothelial cells. Despite the deterioration of the hexagonal structure of the cells, the compensatory polymegatism has not yet developed to predict the order in which the damage will develop.

Morbid obesity is a state of low-grade systemic inflammation caused by the release of inflammatory cytokines, adipokines, and reactive oxygen species.[14] We think that the loss of hexagonality and increase in corneal thickness observed in morbidly obese patients in our study may be related to this. Although patients with abnormal sedimentation and C-reactive protein values were excluded from the study, correlation analyses of these parameters with endothelial cell properties could not be performed. On the other hand, in regression analyses, no significant difference was detected between the level of obesity and endothelial cell parameters.

In our study, no significant difference has been found in IOP between the two groups. However, in morbidly obese patients, an increase in episcleral venous pressure and decreased posttrabecular drainage of the aqueous humor may be observed secondary to increased venous pressure.[15] Although no significant difference was detected between the two groups, fluctuations due to diurnal rhythm and/or lying position were not analyzed. Thus, the mechanical pressure on the endothelial cells due to IOP fluctuations and morphological changes in the endothelial cells may have started. Although it seems unlikely that obesity alone will cause endothelial cell damage and result in corneal decompensation, it has been shown that possible IOP elevations and optic nerve damage may be associated with obesity, especially in patients of advanced age and with glaucomatous pathology.[16]

Since correlation analyses of endothelial cell parameters and systemic inflammatory markers were not performed in our study, it cannot be commented on whether there is a direct relationship. Although any parameter in the blood tests that were outside normal limits was considered an exclusion criterion, the correlation analyses could not be performed. Another limitation is that diurnal measurements were not taken, especially to detect fluctuations in IOP. To overcome this limitation, all participants were measured at early and fixed times of the day, but the variations during the day were not detected.

## CONCLUSION

As a result, although BMI has the effect of changing corneal morphology, this change is not correlated with an increase in BMI. For more certain results, studies on larger patient groups are needed.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of the Balıkesir University Faculty of Medicine Clinical Researches Ethics Committee (Date: 09.10.2019, Decision No: 2019/136).

**Informed Consent:** The written informed consents were obtained. All patients signed and free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial disclosure:** The authors declared that they have no financial relationship.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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